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1-Substituted Cyclopentylamines from Nitriles and Tetramethylenebismagnesium Dibromide in the Presence of Ti(O*i*Pr)$_4$

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Various 1-substituted cyclopentylamines (25 examples, 10–89 % yield) have been prepared according to a one-pot procedure by the addition of tetramethylenebismagnesium dibromide in the presence of Ti(O*i*Pr)$_4$ to aliphatic, aromatic and heteroaromatic nitriles, respectively.

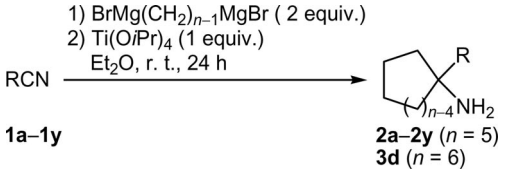
Introduction

Synthetic approaches to 1-alkylsubstituted cycloalkylamines are the same as those to acyclic primary *tert*-alkylamines.[1] The situation is quite different in the case of 1-aryl- and especially 1-hetaryl-substituted cycloalkylamines: the most general and widely used method, the Ritter reaction, fails for these compounds.[2] The poor ability of 1-arylcycloalkanols or 1-arylcycloalkenes to form the corresponding amides in the Ritter reaction with HCN, MeCN or ClCH$_2$CN is apparently due to the low electrophilicity of the intermediate carbenium ions. Only two general methods are known for the synthesis of 1-arylsubstituted cycloalkylamines. The first one is the Curtius degradation of acyl azides, prepared from the respective carboxylic acids by employing the usual mixed anhydride protocol.[3] An obvious drawback of this approach is the poor availability of 1-arylcycloalkanecarboxylic acids. The second method is the transformation of a 1-arylcycloalkanol or a corresponding alkene into an azide by treatment with hydroazotic acid or its equivalent with subsequent reduction.[4] This method is not likely to be suitable for the synthesis of 1-hetarylcyloalkylamines containing an acid-sensitive hetaryl fragment such as furan or pyrrole.

Results and Discussion

As we have previously reported, acyclic primary *tert*-alkylamines can be prepared by twofold addition of Grignard reagents to nitriles in the presence of Ti(O*i*Pr)$_4$.[5] This transformation can be considered as the aza analogue of the formation of tertiary alcohols by the twofold addition of Grignard reagents to esters. Since 1-substituted cycloalkanols can be prepared analogously from esters employing bifunctional Grignard reagents, i.e. α,ω-bis(bromomagnesio)alkanes,[6] it was of interest to test whether 1-substituted cycloalkylamines can also be obtained from nitriles and 1,4-bis(bromomagnesio)butane and probably its higher homologues according to the protocol developed for acyclic primary *tert*-alkylamines.

Indeed, propionitrile (**1a**), cyclopropanecarbonitrile (**1c**), *o*-tolunitrile (**1e**) and 4-(trifluoromethyl)benzonitrile (**1l**) upon reaction with 1,4-bis(bromomagnesio)butane, prepared from 1,4-dibromobutane with metallic magnesium in the presence of titanium tetraisopropoxide, furnished 1-ethylcyclopentylamine (**2a**), 1-cyclopropylcyclopentylamine (**2c**), 1-(*o*-tolyl)cyclopentylamine (**2e**) and 1-[3-(trifluoromethyl)phenyl]cyclopentylamine (**2l**) in low yields (31, 23, 20 and 25%, respectively). Moderate to good yields (40–80%) were obtained from isobutyronitrile (**1b**), benzonitrile (**1d**) and various *p*-substituted benzonitriles (Scheme 1, Table 1). The low yield of 1-(4-bromophenyl)cyclopentylamine (**2j**) (28%) is probably due to a competing transmetallation reaction.



Scheme 1. Synthesis of 1-substituted cycloalkylamines. For details see Table 1.

As for hetarenecarbonitriles, electron-deficient pyridinecarbonitriles **1m**–**o** gave the corresponding amines **2m**–**o** in low yields, while quinoline-2-carbonitrile (**1p**) produced the product **2p** in moderate yield (56%) and in the case of pyr-

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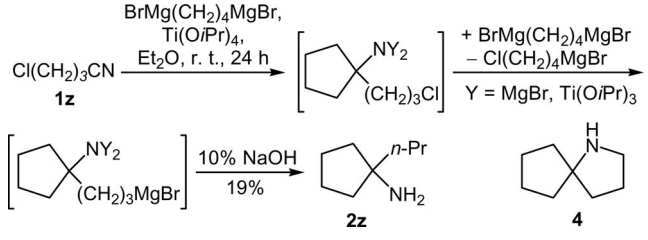
Table 1. 1-Substituted cycloalkylamines **2**, **3** from nitriles **1** and α,ω-bis(bromomagnesio)alkanes (see Scheme 1).

Nitrile **1**	R	*n*	Product	% Yield
a	Et	5	**2a**	31
b	*i*Pr	5	**2b**	71
c	cPr	5	**2c**	23
d	Ph	5	**2d**	40
e	2-MeC_6H_4	5	**2e**	20
f	4-MeC_6H_4	5	**2f**	43
g	4-$MeOC_6H_4$	5	**2g**	76
h	4-$EtOC_6H_4$	5	**2h**	80
i	3,4-$(MeO)_2C_6H_3$	5	**2i**	56
j	4-BrC_6H_4	5	**2j**	28
k	3-$CF_3C_6H_4$	5	**2k**	55
l	4-$CF_3C_6H_4$	5	**2l**	25
m	pyrid-2-yl	5	**2m**	10
n	pyrid-3-yl	5	**2n**	20
o	pyrid-4-yl	5	**2o**	21
p	quinolin-2-yl	5	**2p**	56
q	pyrimidin-2yl	5	**2q**	0
r	fur-2-yl	5	**2r**	47
s	2-methylfur-3-yl	5	**2s**	61
t	benzofur-2-yl	5	**2t**	67
u	thien-2-yl	5	**2u**	44
v	2-methyloxazol-4-yl	5	**2v**	59
w	5-methylisoxazol-3-yl	5	**2w**	47
x	1-methylpyrazol-3-yl	5	**2x**	89
y	1-methylpyrazol-5-yl	5	**2y**	67
d	Ph	6	**3d**	13

imidine-2-carbonitrile (**1q**) no amine **2q** was formed at all. Electron-rich hetarenecarbonitriles such as furan-2-carbonitrile (**1r**), 2-methylfuran-3-carbonitrile (**1s**), benzofuran-2-carbonitrile (**1t**) and thiophene-2-carbonitrile (**1u**) furnished the corresponding amines **2r**–**u** in moderate yields (44–67%). Some other hetarenecarbonitriles **1v**–**y** provided 1-hetarylcyclopentylamines **2v**–**y** in moderate to high yields, and the best yield (89%) was obtained in the case of 1-methyl-1*H*-pyrazole-3-carbonitrile (**1x**).

As 4-chlorobutyronitrile (**1z**) reacts with phenylmagnesium bromide to give 2,2-diphenylpyrrolidine (42%), tetramethylenebismagnesium dibromide was expected to react with nitrile **1z** to yield 1-azaspiro[4.4]nonane (**4**), but the only isolated amine was 1-propylcyclopentylamine (**2z**) (19%), which can be produced through a transmetallation reaction (Scheme 2).

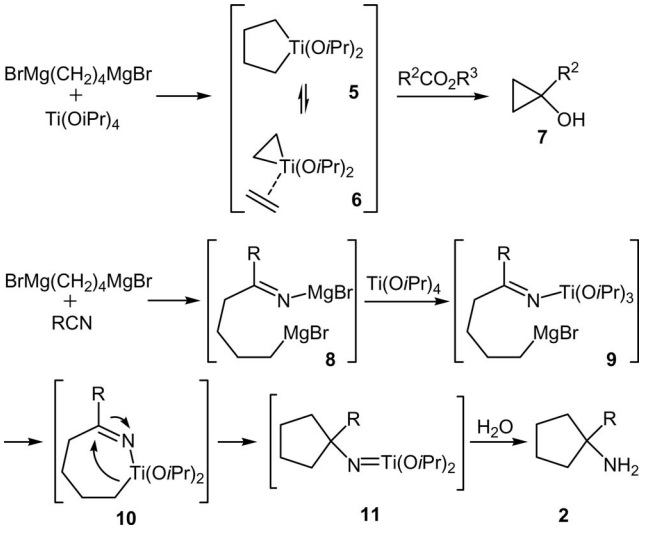


Scheme 2. Reaction of 4-chlorobutyronitrile (**1z**) with tetramethylenebismagnesium dibromide.

Pentamethylenebismagnesium dibromide in its reaction with benzonitrile (**1d**) under the same conditions gave 1-phenylcyclohexylamine (**3d**), yet in only 13% yield and with greater difficulty in the isolation of the product. 4-Ethoxybenzonitrile (**1h**), which provided 1-(4-ethoxyphenyl)cyclopentylamine (**2h**) in very good yield (80%), with pentamethylenebismagnesium dibromide produced a complex mixture, from which the desired amine could not be isolated.

Conclusions

Mechanistically, this newly observed reaction of nitriles is quite remarkable. It is known that tetramethylenebismagnesium dibromide rapidly reacts with $Ti(OiPr)_4$ to initially furnish titanacyclopentane **5**,[7] which, by analogy with the known bis(cyclopentadienyl)titanacyclopentane,[8] apparently equilibrates with the titanacyclopropane-ethylene complex **6**. With esters such as methyl pentanoate, mixture **5/6** reacts as a 1,2-dicarbanion equivalent[7] to yield 1-substituted cyclopropanols, albeit in moderate yields. When the order of reagent addition is different, tetramethylenebismagnesium dibromide reacts with nitriles as a typical 1,4-dicarbanionic building block due to the double transmetallation reaction with $Ti(OiPr)_4$, furnishing the seven-membered cyclic intermediate **10**, and subsequent ring contraction to 1-substituted cyclopentylamines **2**.[9] By analogy, the reaction of pentamethylenebismagnesium dibromide and $Ti(OiPr)_4$ with a nitrile would have to proceed via an eight-membered ring intermediate analogous to **10**, and the less favorable formation of eight-membered rings may be the reason for the low yield of **3d** from **1d** (Scheme 3).



Scheme 3. Varying behavior of a tetramethylenebismagnesium dibromide.

Experimental Section

General Remarks: NMR spectra were recorded with a Bruker DPX 300 instrument at 300 (^1H) and 75 (^{13}C and DEPT) MHz. All spectra were calibrated against tetramethylsilane as an internal standard (δ = 0 ppm) or the signals of residual protons of deuterated solvents: δ = 7.26 for $CHCl_3$, δ = 2.50 for $[D_5]DMSO$. Multiplicities of signals are described as follows: s = singlet, d = doublet, t = triplet, q = quadruplet, m_c = centered multiplet. Coupling con-

stants (J) are given in Hz; J values in ^{13}C NMR spectra refer to ^{13}C-^{19}F couplings. Mass spectra were recorded with a Finnigan MAT 95 spectrometer. Analytical TLC was performed on Machery–Nagel ready-to-use plates AluGram® Sil G/UV$_{254}$. Detection was achieved by development with molybdatophosphoric acid solution (5% in EtOH). Column chromatography: Merck silica gel 60 (0.063–0.200 mm). Elemental analyses were carried out with a CHN-analyzer Hewlett–Packard 185B. In the case of compounds with two or more nitrogen atoms, the hydrochlorides often contain water. Solvents were purified by standard procedures.

General Procedure for the Synthesis of 1-Substituted Cyclopentylamines 2a–y and 1-Phenylcyclohexylamine (3d): To a two-phase mixture of tetramethylenebismagnesium dibromide or pentamethylenebismagnesium dibromide obtained from 1,4-dibromobutane (4.32 g, 20 mmol) or 1,5-dibromopentane (4.6 g, 20 mmol) and magnesium turnings (1.06 g, 44 mmol) in Et_2O (50 mL) according to a standard procedure, a solution of the respective nitrile (10 mmol) in Et_2O (10 mL) was added at room temp. After stirring for an additional 30 min, a solution of Ti(O*i*Pr)$_4$ (2.84 g, 10 mmol) in Et_2O (5 mL) was added. Stirring was continued at r. t. for 24 h, then 10% aq. NaOH (30 mL) was added. The mixture was filtered and the filtrate extracted with diethyl ether (3 × 30 mL). The combined ether phases were extracted three times with dilute (5%) aq. HCl. The combined aqueous layers were washed with CH_2Cl_2 (1 × 10 mL), made basic by addition of 10% aq. NaOH and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were dried (Na_2SO_4), and a few mL of 6 M HCl in Et_2O or *i*PrOH were added to acidify the solution. The solution was concentrated to dryness to leave the crude amine hydrochloride, which was purified by column chromatography on silica gel, eluting with chloroform/methanol and/or by recrystallization (*i*PrOH/Et_2O).

Analytical Data of New Compounds

1-Isopropylcyclopentylamine Hydrochloride (2b): From isobutyronitrile (**1b**) (690 mg, 10 mmol) the product **2b** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (1.17 g, 71%), m.p. > 250 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.11 (d, J = 6.6 Hz, 6 H), 1.58–1.82 (m, 4 H), 1.89–2.14 (m, 5 H), 8.25 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 18.3 (2 CH_3), 24.9 (2 CH_2), 35.6 (2 CH_2), 36.7 (CH), 69.7 (C) ppm. MS (DCI): m/z (%) = 128 (100) [M – Cl]$^+$. $C_8H_{17}N$·HCl (163.69): calcd. C 58.70, H 11.08, N 8.56; found C 58.98, H 11.14, N 8.39.

1-(4-Methylphenyl)cyclopentylamine Hydrochloride (2f): From *p*-tolunitrile (**1f**) (1.17 g, 10 mmol) the product **2f** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (910 mg, 43%), m.p. 235–237 °C. The amine **2f** has previously been reported, but without any experimental data.[10] ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.77 (m_c, 2 H), 1.93–2.16 (m, 4 H), 2.24–2.38 (m, 2 H), 2.34 (s, 3 H), 7.14 (d, J = 7.8 Hz, 2 H), 7.44 (d, J = 8.1 Hz, 2 H), 8.52 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.5 (CH_3), 23.2 (2 CH_2), 38.0 (2 CH_2), 67.3 (C), 127.0 (2 CH), 129.6 (2 CH), 137.6 (C), 138.2 (C) ppm. MS (70 eV): m/z (%) = 175 (15) [M – HCl]$^+$, 146 (100), 118 (30), 41 (30), 39 (39). $C_{12}H_{17}N$·HCl (211.73): calcd. C 68.07, H 8.57, N 6.62; found C 68.07, H 8.56, N 6.72.

1-(4-Methoxyphenyl)cyclopentylamine Hydrochloride (2g): From 4-methoxybenzonitrile (**1g**) (1.33 g, 10 mmol) the product **2g** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (1.74 g, 76%), m.p. > 250 °C. The amine **2g** has previously been reported, but without any experimental data.[10] ^1H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.70 (m_c, 2 H), 1.91–2.16 (m, 4 H), 2.30 (m_c, 2 H), 3.79 (s, 3 H), 6.88 (d, J = 9.0 Hz, 2 H), 7.49 (d, J = 8.7 Hz, 2 H), 8.64 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 23.3 (2 CH_2), 38.0 (2 CH_2), 55.8 (CH_3), 65.7 (C), 115.2 (2 CH), 128.6 (2 CH), 133.7 (C), 159.6 (C) ppm. MS (70 eV): m/z (%) = 191 (13) [M – HCl]$^+$, 162 (100), 134 (24), 39 (43), 36 (47). $C_{12}H_{17}NO$·HCl (227.73): calcd. C 63.29, H 7.97, N 6.15; found C 63.23, H 7.94, N 6.11.

1-(4-Ethoxyphenyl)cyclopentylamine Hydrochloride (2h): From 4-ethoxybenzonitrile (**1h**) (1.47 g, 10 mmol) the product **2h** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (1.93 g, 80%), m.p. 205–207 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.42 (t, J = 7.5 Hz, 3 H), 1.75 (m_c, 2 H), 1.90–2.13 (m, 4 H), 2.28 (m_c, 2 H), 4.02 (q, J = 6.5 Hz, 2 H), 6.85 (d, J = 8.7 Hz, 2 H), 7.47 (d, J = 8.7 Hz, 2 H), 8.47 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 15.2 (CH_3), 23.1 (2 CH_2), 38.0 (2 CH_2), 63.7 (CH_2), 67.2 (C), 115.0 (2 CH), 128.5 (2 CH), 132.4 (C), 159.1 (C) ppm. MS (70 eV): m/z (%) = 205 (17) [M – HCl]$^+$, 176 (100), 148 (37), 36 (33), 39 (28). $C_{13}H_{19}NO$·HCl (241.76): calcd. C 64.59, H 8.34, N 5.79; found C 64.37, H 8.32, N 5.99.

1-(3,4-Dimethoxyphenyl)cyclopentylamine Hydrochloride (2i): From 3,4-dimethoxybenzonitrile (**1i**) (1.63 g, 10 mmol) the product **2i** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (1.46 g, 56%), m.p. 215–217 °C. ^1H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.71 (m_c, 2 H), 1.93–2.19 (m, 4 H), 2.29 (m_c, 2 H), 3.79 (s, 3 H), 3.86 (s, 3 H), 6.84 (d, J = 9.0 Hz, 1 H), 6.97 (dd, J = 9.0 and 2.4 Hz, 1 H), 7.34 (d, J = 2.1 Hz, 1 H), 8.67 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 23.3 (2 CH_2), 37.9 (2 CH_2), 56.2 (CH_3), 56.5 (CH_3), 66.0 (C), 111.6 (CH), 112.1 (CH), 118.9 (CH), 134.1 (C), 149.4 (C), 149.6 (C) ppm. MS (70 eV): m/z (%) = 221 (18) [M – Cl]$^+$, 192 (100), 162 (18), 41 (26), 36 (24). $C_{13}H_{19}NO_2$·HCl (256.76): calcd. C 60.58, H 7.82, N 5.43; found C 60.33, H 7.70, N 5.36.

1-(4-Bromophenyl)cyclopentylamine Hydrochloride (2j): From 4-bromobenzonitrile (**1j**) (1.82 g, 10 mmol) the product **2j** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (774 mg, 28%), m.p. > 250 °C. ^1H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.71 (m_c, 2 H), 1.93–2.17 (m, 4 H), 2.34 (m_c, 2 H), 7.54 (d, J = 8.7 Hz, 2 H), 7.46 (d, J = 8.7 Hz, 2 H), 8.84 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 23.0 (2 CH_2), 37.8 (2 CH_2), 67.2 (C), 123.1 (2 CH), 129.2 (2 CH), 132.1 (C), 139.1 (C) ppm. MS (DCI): m/z (%) = 242/240 (100) [M – Cl]$^+$. $C_{11}H_{14}BrN$·HCl (276.60): calcd. C 47.77, H 5.47, N 5.06; found C 48.20, H 5.41, N 5.19.

1-[(3-Trifluoromethyl)phenyl]cyclopentylamine Hydrochloride (2k): From 3-trifluoromethylbenzonitrile (**1k**) (1.71 g, 10 mmol) the product **2k** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (1.45 g, 55%), m.p. 197–199 °C. ^1H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.75 (m_c, 2 H), 1.98–2.20 (m, 4 H), 2.41 (m_c, 2 H), 7.58–7.65 (m, 2 H), 7.85 (s, 1 H), 7.85–7.95 (m, 1 H), 8.61 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 23.5 (2 CH_2), 38.3 (2 CH_2), 65.9 (C), 124.0 (q, $^3J_{C,F}$ = 4 Hz, CH), 124.7 (q, $^1J_{C,F}$ = 270 Hz, CF_3), 125.3 (q, $^3J_{C,F}$ = 4 Hz, CH), 130.0 (CH), 130.4 (q, $^2J_{C,F}$ = 32 Hz, 1 C), 131.5 (CH), 143.2 (C) ppm. MS (ESI): m/z (%) = 230 (50) [M – Cl]$^+$, 213 (100) [M – HCl – NH_2]$^+$. $C_{12}H_{14}F_3N$·HCl (265.71): calcd. C 54.27, H 5.69, N 5.27; found C 54.10, H 5.82, N 5.26.

1-[4-(Trifluoromethyl)phenyl]cyclopentylamine Hydrochloride (2l): From 4-(trifluoromethyl)benzonitrile (**1l**) (1.71 g, 10 mmol) the product **2l** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (652 mg, 25%), m.p. 217–220 °C. The amine **2l** has previously been reported, but without any experimental data.[11] ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.75–2.11 (m, 6 H), 2.21–2.36 (m, 2 H), 7.63 (d, J = 9.0 Hz, 2 H), 7.70 (d, J = 8.7 Hz, 2 H), 8.61 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 22.9 (2

CH_2), 37.8 (2 CH_2), 67.4 (C), 124.2 (q, $^1J_{C,F}$ = 270 Hz, CF_3), 126.0 (q, $^3J_{C,F}$ = 4 Hz, 2 CH), 127.9 (2 CH), 131.1 (q, $^2J_{C,F}$ = 30 Hz, 1 C), 143.8 (C) ppm. MS (ESI): *m*/*z* (%) = 230 (64) $[M - Cl]^+$, 213 (100) $[M - HCl - NH_2]^+$. $C_{12}H_{14}F_3N$·HCl (265.71): calcd. C 54.27, H 5.69, N 5.27; found C 54.33, H 5.67, N 5.26.

1-(Pyrid-2-yl)cyclopentylamine Dihydrochloride (2m): From pyridine-2-carbonitrile (**1m**) (1.04 g, 10 mmol) the product **2m** was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 3:1 and subsequent recrystallization (*i*PrOH/Et_2O) as a colorless solid (0.24 g, 10%), m.p. >250 °C. ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.83 (m_c, 2 H), 2.05 (m_c, 2 H), 2.2–2.3 (m, 4 H), 7.36 (dd, *J* = 7.8 and 4.8 Hz, 1 H), 7.69 (br. d, *J* = 7.8 Hz, 1 H), 7.87 (dt, *J* = 7.8 and 1.8 Hz, 1 H), 8.59 (br. d, *J* = 4.8 Hz, 1 H), 8.84 (br. s, 4 H) ppm. ^{13}C NMR (75 MHz, D_2O, 25 °C): δ = 23.8 (2 CH_2), 38.1 (2 CH_2), 66.7 (C), 124.8 (CH), 127.0 (CH), 145.2 (CH) 146.0 (CH), 154.7 (C) ppm. MS (ESI): *m*/*z* (%) = 163 (100) $[M - Cl - Cl]^+$. $C_{10}H_{14}N_2$·2HCl·$^1/_3H_2O$ (240.56): calcd. C 49.92, H 6.96, N 11.64; found C 49.98, H 6.96, N 11.94.

1-(Pyrid-3-yl)cyclopentylamine Dihydrochloride (2n): From pyridine-3-carbonitrile (**1n**) (1.04 g, 10 mmol) the product **2n** was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 4:1 and subsequent recrystallization (*i*PrOH/Et_2O) as a colorless solid (470 mg, 20%), m.p. 234–235 °C. The amine **2n** has previously been reported, but without any experimental data.[12] ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.80 (m_c, 2 H), 2.0–2.3 (m, 4 H), 2.50 (m_c, 2 H), 8.09 (dd, *J* = 8.3 and 5.6 Hz, 1 H), 8.85–8.95 (m, 2 H), 9.15 (d, *J* = 2.0 Hz, 1 H), 9.28 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, D_2O, 25 °C): δ = 23.0 (2 CH_2), 37.7 (2 CH_2), 65.2 (C), 128.5 (CH), 140.6 (CH), 140.7 (C) 142.4 (CH), 145.9 (CH) ppm. MS (ESI): *m*/*z* (%) = 163 (100) $[M - Cl - Cl]^+$. $C_{10}H_{14}N_2$·2HCl·1/2H_2O (244.16): calcd. C 49.19, H 7.02, N 11.47; found C 49.41, H 6.76, N 11.23.

1-(Pyrid-4-yl)cyclopentylamine Dihydrochloride (2o): From pyridine-3-carbonitrile (**1o**) (1.04 g, 10 mmol) the product **2o** was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 3:1 and subsequent recrystallization (*i*PrOH/Et_2O) as a colorless solid (500 mg, 21%), m.p. 245–250 °C. The amine **2o** has previously been reported, but without any experimental data.[12] ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.85 (m_c, 2 H), 2.0–2.2 (m, 4 H), 2.42 (m_c, 2 H), 8.35 (d, *J* = 5.7 Hz, 2 H), 9.02 (d, *J* = 5.7 Hz, 2 H), 9.50 (br. s, 4 H) ppm. ^{13}C NMR (75 MHz, D_2O, 25 °C): δ = 24.4 (2 CH_2), 39.5 (2 CH_2), 66.7 (C), 125.2 (2 CH), 142.6 (2 CH), 161.4 (C) ppm. MS (ESI): *m*/*z* (%) = 163 (100) $[M - Cl - Cl]^+$. $C_{10}H_{14}N_2$·2HCl (234.07): calcd. C 51.08, H 6.86, N 11.91; found C 51.05, H 7.12, N 11.73.

1-(Quinolin-2-yl)cyclopentylamine Hydrochloride (2p): From quinoline-2-carbonitrile[13] (**1p**) (770 mg, 5 mmol), the product **2p** was obtained as a colorless solid (700 mg, 56%), m.p. > 250 °C. An analytically pure sample was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 4:1 and subsequent recrystallization (*i*PrOH/Et_2O). ^{1}H NMR (300 MHz, [D_6]-DMSO/CCl_4, 25 °C): δ = 1.89 (m_c, 2 H), 2.12 (m_c, 2 H), 2.2–2.4 (m, 4 H), 7.59 (m, 1 H), 7.7–7.8 (m, 2 H), 7.94 (d, *J* = 8.0 Hz, 1 H), 8.04 (d, *J* = 8.0 Hz, 1 H), 8.38 (d, *J* = 8.7 Hz, 1 H), 8.92 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 24.5 (2 CH_2), 38.4 (2 CH_2), 66.8 (C), 117.9 (CH), 126.4 (CH), 126.7 (C), 127.4 (CH), 128.9 (CH), 129.5 (CH), 137.3 (CH), 145.7 (C), 160.3 (C) ppm. MS (ESI): *m*/*z* (%) = 213 (100) $[M - Cl]^+$. $C_{14}H_{16}N_2$·HCl (248.75): calcd. C 67.60, H 6.89, N 11.26; found C 67.52, H 7.00, N 11.01.

1-(Fur-2-yl)cyclopentylamine Hydrochloride (2r): From furan-2-carbonitrile (**1r**) (930 mg, 10 mmol) the product **2r** was obtained as a colorless solid (880 mg, 47%), m.p. 209–210 °C. An analytically pure sample was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 10:1 and subsequent recrystallization (*i*PrOH/Et_2O). ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.58–1.73 (m_c, 2 H), 1.89–2.02 (m_c, 2 H), 2.12–2.25 (m, 4 H), 6.38 (dd, *J* = 3.3 and 1.7 Hz, 1 H), 6.50 (d, *J* = 3.3 Hz, 1 H), 7.53 (d, *J* = 1.7 Hz, 1 H), 8.93 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 23.1 (2 CH_2), 36.1 (2 CH_2), 60.8 (C), 107.1 (CH), 110.3 (CH), 142.2 (CH) 153.6 (C) ppm. MS (ESI): *m*/*z* (%) = 152 (100) $[M - Cl]^+$. $C_9H_{13}NO$·HCl (187.08): calcd. C 57.60, H 7.52, N 7.46; found C 57.29, H 7.64, N 7.21.

1-(2-Methylfur-3-yl)cyclopentylamine Hydrochloride (2s): From 2-methylfuran-3-carbonitrile (**1s**) (1.07 g, 10 mmol), obtained from ethyl 2-methylfuran-3-carboxylate by a standard procedure,[14] the product **2s** was obtained as a colorless solid (1.230 g, 61%), m.p. 204–205 °C. An analytically pure sample was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 10:1 and subsequent recrystallization (*i*PrOH/Et_2O). ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.63–1.75 (m_c, 2 H), 1.93–2.06 (m, 4 H), 2.26–2.37 (m_c, 2 H), 2.41 (s, 3 H), 6.51 (d, *J* = 2.0 Hz, 1 H), 7.28 (d, *J* = 2.0 Hz, 1 H), 8.53 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 13.5 (CH_3), 22.7 (2 CH_2), 36.9 (2 CH_2), 60.4 (C), 111.4 (CH), 119.8 (C), 139.4 (CH) 148.0 (C) ppm. MS (ESI): *m*/*z* (%) = 166 (35) $[M - Cl]^+$. $C_{10}H_{15}NO$·HCl (201.09): calcd. C 59.55, H 8.00, N 6.94; found C 59.41, H 8.04, N 6.80.

1-(Benzofur-2-yl)cyclopentylamine Hydrochloride (2t): From benzofuran-2-carbonitrile (**1t**) (1.43 g, 10 mmol) the product **2t** was obtained after recrystallization (*i*PrOH/Et_2O) as a colorless solid (1.60 g, 67%), m.p. 224–226 °C. ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.78 (m_c, 2 H), 2.04 (m_c, 2 H), 2.25–2.35 (m, 4 H), 6.97 (s, 1 H), 7.2–7.3 (m, 2 H), 7.47 (br. d, *J* = 8.0 Hz, 1 H), 7.59 (br. d, *J* = 7.7 Hz, 1 H), 9.18 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 23.5 (2 CH_2), 36.4 (2 CH_2), 61.2 (C), 103.6 (CH), 110.8 (CH), 121.0 (CH), 122.7 (CH), 124.2 (CH), 127.5 (C), 154.1 (C), 156.4 (C) ppm. MS (ESI): *m*/*z* (%) = 202 (47) $[M - Cl]^+$. $C_{13}H_{15}NO$·HCl (237.09): calcd. C 65.68, H 6.78, N 5.89; found C 65.42, H 6.89, N 5.84.

1-(Thien-2-yl)cyclopentylamine Hydrochloride (2u): From thiophene-2-carbonitrile (**1u**) (1.09 g, 10 mmol) the product **2u** was obtained as a colorless solid (890 mg, 44%), m.p. 212–213 °C. An analytically pure sample was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 10:1 and subsequent recrystallization (*i*PrOH/Et_2O). ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.72 (m_c, 2 H), 2.00 (m_c, 2 H), 2.20 (m_c, 2 H), 2.36 (m_c, 2 H), 7.02 (dd, *J* = 5.1 and 3.6 Hz, 1 H), 7.36 (dd, *J* = 5.1 and 0.9 Hz, 1 H), 7.40 (dd, *J* = 3.6 and 0.9 Hz, 1 H), 8.94 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 22.7 (2 CH_2), 38.9 (2 CH_2), 62.3 (C), 124.7 (CH), 126.2 (CH), 127.0 (CH) 144.9 (C) ppm. MS (ESI): *m*/*z* (%) = 168 (64) $[M - Cl]^+$. $C_9H_{13}NS$·HCl (203.05): calcd. C 53.06, H 6.93, N 6.88; found C 53.07, H 7.03, N 6.74.

1-(2-Methyloxazol-4-yl)cyclopentylamine Hydrochloride (2v): From 2-methyloxazole-4-carbonitrile[15] (**1v**) (1.08 g, 10 mmol) the product **2v** was obtained as a brown solid (1.20 g, 59%), m.p. 200–202 °C. An analytically pure sample was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 4:1 and subsequent recrystallization (*i*PrOH/Et_2O). ^{1}H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.68 (m_c, 2 H), 1.91 (m_c, 2 H), 2.05–2.15 (m, 4 H), 2.41 (s, 3 H), 7.92 (s, 1 H), 8.76 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 13.4

(CH_3), 23.3 (2 CH_2), 36.6 (2 CH_2), 60.2 (C), 135.1 (CH), 141.3 (C), 160.7 (C) ppm. MS (ESI): *m*/*z* (%) = 167 (100) $[M - Cl]^+$, 150 (36) $[M - HCl - NH_2]^+$. $C_9H_{14}N_2O{\cdot}HCl{\cdot}1/4H_2O$ (207.19): calcd. C 52.17, H 7.54, N 13.52; found C 52.20, H 7.57, N 13.18.

1-(5-Methylisoxazol-3-yl)cyclopentylamine Hydrochloride (2w): From 5-methylisoxazole-3-carbonitrile[16] (**1w**) (1.08 g, 10 mmol) the product **2w** was obtained as a brown solid (950 mg, 47%), m.p. 161–163 °C. An analytically pure sample was obtained after column chromatography on silica gel, eluting with chloroform/methanol, 4:1 and subsequent recrystallization (*i*PrOH/Et_2O). ^1H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.80 (m_c, 2 H), 2.05 (m_c, 2 H), 2.2–2.3 (m, 4 H), 2.53 (s, 3 H), 6.66 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 11.9 (CH_3), 23.3 (2 CH_2), 36.6 (2 CH_2), 60.4 (C), 100.3 (CH), 164.9 (C), 169.6 (C) ppm. MS (ESI): *m*/*z* (%) = 167 (44) $[M - Cl]^+$, 150 (100) $[M - HCl - NH_2]^+$. $C_9H_{14}N_2O{\cdot}HCl{\cdot}1/4H_2O$ (207.19): calcd. C 52.17, H 7.54, N 13.52; found C 52.49, H 7.52, N 13.20.

1-(1-Methyl-1*H*-pyrazol-3-yl)cyclopentylamine Hydrochloride (2x): From 1-methyl-1*H*-pyrazole-3-carbonitrile[17] (**1x**) (1.07 g, 10 mmol) the product **2x** was obtained as a colorless solid (1.80 g, 89%), m.p. 208–210 °C. An analytically pure sample was obtained after recrystallization (*i*PrOH/Et_2O). ^1H NMR (300 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 1.8 (m_c, 2 H), 1.93 (m_c, 2 H), 2.05–2.30 (m, 4 H), 3.85 (s, 3 H), 6.45 (br. s, 1 H), 7.58 (br. s, 1 H), 8.66 (br. s, 3 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 23.2 (2 CH_2), 37.1 (2 CH_2), 38.3 (CH_3), 61.5 (C), 102.9 (CH), 131.6 (CH), 152.4 (C) ppm. MS (ESI): *m*/*z* (%) = 166 (72) $[M - Cl]^+$, 149 (100) $[M - HCl - NH_2]$. $C_9H_{15}N_3{\cdot}HCl$ (201.70): calcd. C 53.59, H 8.00, N 17.58; found C 54.15, H 8.03, N 17.46.

1-(1-Methyl-1*H*-pyrazol-5-yl)cyclopentylamine Dihydrochloride (2y): From 1-methyl-1*H*-pyrazole-5-carbonitrile[17] (**1y**) (1.07 g, 10 mmol) the product **2y** was obtained as a colorless solid (1.60 g, 67%), m.p. 195–197 °C. An analytically pure sample was obtained after recrystallization (*i*PrOH/Et_2O). ^1H NMR (300 MHz, [D_6]-DMSO/CCl_4, 25 °C): δ = 1.75 (m_c, 2 H), 2.0–2.2 (m, 4 H), 2.45 (m_c, 2 H), 4.04 (s, 3 H), 6.32 (br. s, 1 H), 7.32 (br. s, 1 H), 8.88 (br. s, 3 H), 10.52 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO/CCl_4, 25 °C): δ = 22.9 (2 CH_2), 37.2 (2 CH_2), 59.8 (C), 106.9 (CH), 136.4 (CH), 142.0 (C) ppm. MS (ESI): *m*/*z* (%) = 166 (100) $[M - Cl - HCl]^+$, 149 (90) $[M - HCl - HCl - NH_2]$. $C_9H_{15}N_3{\cdot}2HCl{\cdot}0.2H_2O$ (241.76): calcd. C 44.71, H 7.25; found C 45.22, H 7.27.

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